

Attorney Docket No.: 56476 (71661)  
U.S.S.N.: 09/964,260  
Title: Derivatives of Pyrimido [6,1-] Isoquinolin-4-One  
Inventors: Oxford, et al.  
Filed: September 26, 2001  
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*contd.*  
*A 4*

48. (Amended) A method as claimed in any of claims 44 to 45, wherein the animal is human.

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### REMARKS

The amendments to the specification are to correct informalities in the application as filed and do not introduce new matter. The amendments to the claims are made solely to remove improper multiple dependencies and without prejudice to pursuing claims of similar scope in this or related applications.

### CONCLUSION

Applicants submit that all claims are allowable as written and respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicants' agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned agent of record.

Respectfully submitted

Date: May 7, 2002

By: \_\_\_\_\_

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### **Marked-Up Sections of Specification Showing Changes Being Made**

#### **At page 2, lines 1-5:**

The potential adverse effects of a PDE III/IV inhibitor (e.g., nausea and vomiting, gastric acid secretion, cardiovascular effects such as increase cardiac contractility, vasodilation and potential arrhythmogenic activity) should be avoidable with a compound that is directly delivered to the lungs by inhalation. It is desirable that the substance is long acting and non-irritant [and has a taste which is not so unpleasant as to have any adverse effect on patient compliance].

#### **At page 2, lines 14-18:**

As described by De Souza *et al.* and in GB-A-1597717, trequinsin has valuable pharmacological properties, and can be administered to human subjects suffering from, for example, respiratory disorders. However, it is unsuitable for administration by inhalation because [of its bitter taste and] *in vitro* data indicate its persistence of action is less than desirable.

#### **At page 2, lines 20-22:**

It has now been found that it is possible to design certain pyrimido [6,1-a] isoquinolin-4-one derivatives which are PDE inhibitors, which have a longer duration of action relative to trequinsin and other useful properties [such as improved taste].

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**Marked-Up Version of Claims Showing Changes Being Made**

**IN THE CLAIMS**

47. (Amended) A method as claimed in any one of claims 43-45 [46], wherein the compound is administered by aerosol.

48. (Amended) A method as claimed in any of claims 43 to 45 [47], wherein the animal is human.